The Present Invention

The present invention is directed to improved compositions and methods for topical application to animal subjects, wherein the compositions comprise not only at least one irritant ingredient in an amount capable of inducing skin irritation in a subject, but also an anti-irritant amount of aqueous-soluble divalent calcium cation and at least one aqueous-ionizable counter-anionic species.

In an exemplary embodiment as recited in the amended claims, the concentration of calcium cation is at least about 1.8% by weight. In yet another embodiment, the concentration of calcium cation is about 1.8% to about 17.6% by weight. In still another embodiment, the concentration of calcium cation is about 4.4% to about 8.8% by weight. *See* presently pending claims 1 and 4-5.

The 35 U.S.C. §112, First Paragraph, Rejection

Claim 7 stands rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comport with the written description requirement. Specifically, the Patent Office asserts that the application fails to provide a proper written description for qualitative determination of mean cumulative irritation as set forth in claim 7. This rejection is respectfully traversed and withdrawal thereof is requested.

During the telephone interview with the Examiner, Applicants' undersigned representative pointed out that language referenced in asserting this rejection was included within the originally filed specification, both in the claims and elsewhere in the detailed description. For example, see originally filed claim 6, which was canceled by way of a previous amendment. Also see page 22, line 17, to page 23, line 10, and the discussion of exemplifying clinical studies starting on the top of page 30. The Examiner indicated that this information would be considered in overcoming the rejection when Applicants' response is filed. In view thereof, Applicants request such consideration and withdrawal of the present rejection.

The 35 U.S.C. §112, Second Paragraph, Rejection

Claim 7 also stands rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as the invention. Specifically, the Patent Office asserts that the specification or claims fail to provide a clear standard as to the degree of "inhibiting mean cumulative skin irritation" and a means to determine the same. Further, the Patent Office asserts that claim 7 is indefinite as to the degree of inhibiting and the amount of calcium cation required in the claimed composition. This rejection is respectfully traversed and withdrawal thereof is requested.

During the telephone interview with the Examiner, Applicants' undersigned representative pointed out that language referenced in asserting this rejection was included within the originally filed specification, both in the claims and elsewhere in the detailed description. For example, see originally filed claim 6, which was canceled by way of a previous amendment. Also see page 22, line 17, to page 23, line 10, and the discussion of exemplifying clinical studies starting on the top of page 30. The Examiner indicated that this information would be considered in overcoming the rejection when Applicants' response is filed. In view thereof, Applicants request such consideration and withdrawal of the present rejection.

The 35 U.S.C. §102(e) Rejections

The First Rejection

Claims 1-5, 7, 10, 12, 22, 24, and 116-119 stand rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Daggy et al. (U.S. Patent No. 5,422,101). This rejection is respectfully traversed and withdrawal thereof is requested.

Daggy et al. is directed toward a drink mix composition useful for reducing serum cholesterol levels. The drink mix compositions therein contain psyllium husk, an anion exchange resin, and edible, water-soluble salts present at a level sufficient to reduce the gelation rate of the psyllium husk and anion exchange resin-containing composition when dispersed in an aqueous solution. After dispersion in an aqueous solution, the compositions of Daggy et al. are purportedly ready for ingestion by an individual.

Upon ingestion, Daggy et al. indicate that such drink mix compositions help lower blood cholesterol levels by binding to bile acids in the intestine, which in turn causes an increase in hepatic metabolism of cholesterol to replenish the bile acids lost to complexation with the anion exchange resins. In doing so, Daggy et al. note that an object of the invention described therein is to provide "drink mix compositions which are unflavored or are not highly acidic flavored systems." In addition to the substantial differences between the purported effect of the compositions of Daggy et al. and the skin irritation-reducing effects of the presently claimed compositions, the components of the compositions themselves also differ substantially.

Although the Patent Office asserts that Daggy et al. teach compositions of the present invention, with 0.1 to 50% of the composition comprising a salt such as calcium chloride, calcium sulfate, or calcium citrate malate, and 0.1 to 10% of the composition comprising an acid such as ascorbic acid, malic acid, or tartaric acid, such compositions are not compositions for topical application as recited in the presently pending claims. It is to be noted that the referenced weight percentages are associated only with drink mix compositions of Daggy et al. – not compositions that are dispersed in an aqueous solution such that they are ready for ingestion by an individual. The actual amounts of each of these two components in the final aqueous solution are much lower as discussed with the Examiner during the telephone interview.

Reference is made to Example 2 of Daggy et al. with specific focus on the only calcium-containing suspensions therein, which are denoted by column numbers 4 and 5 in the table encompassed within the discussion of Example 2. Example 2 describes compositions containing hydrated calcium chloride. None of the suspensions denoted therein contain an anti-irritant amount of aqueous-soluble divalent calcium cation.

Based on information therein, the amounts (by weight) of each of the listed components for suspension number 4 are as follows: psyllium – 8.2 grams, cholestyramine – 9.6 grams, citric acid aqueous solution – 0.2 gram (with the amount of citric acid therein being only 0.00008 gram), and hydrated calcium chloride – 0.3 gram (with the amount of calcium cation therein being only 0.081 gram). The total weight of these components is thus 18.3 grams. That mixture was then diluted with water to give a total weight of approximately 498 grams.

In the undiluted dry blend mixture, the amount of calcium cation was only about 0.44% by weight of the dry blend mixture, and in the diluted mixture of all components, the amount of calcium cation was far less – approximating 0.016% by weight of the diluted mixture. Prior to the addition of other components therein, the amount of citric acid in aqueous solution was only 0.0004% by weight of the aqueous solution, a minor amount that became negligible once the diluted mixture of all components was formed. Again, reference is made to the fact that the diluted mixtures of Daggy et al. are those purportedly suitable for consumption.

Based on information therein, the weights of each of the listed components for suspension number 5 are as follows: psyllium – 8.2 grams, cholestyramine – 9.6 grams, citric acid – 0.2 gram (with the amount of citric acid therein being only 0.00008 gram), and hydrated calcium chloride – 0.5 gram (with the amount of calcium cation therein being only 0.135 gram). The total weight of these components is thus 18.5 grams. That mixture was then diluted with water to give a total weight of approximately 498 grams.

In the undiluted dry blend mixture, the amount of calcium cation was only about 0.73% by weight of the dry blend mixture, and in the diluted mixture of all components, the amount of calcium cation was far less – approximating 0.027% by weight of the diluted mixture. Prior to the addition of other components therein, the amount of citric acid in aqueous solution was only 0.0004% by weight of the aqueous solution, a minor amount that became negligible once the diluted mixture of all components was formed. Again, reference is made to the fact that the diluted mixtures of Daggy et al. are those purportedly suitable for consumption.

Even assuming arguendo that a calcium-containing salt (e.g., calcium chloride as exemplified) constitutes as much as 50% by weight of the drink mix compositions described by Daggy et al., there is no indication that the amount of calcium cation in compositions suitable for ingestion and derived from such drink mix compositions (i.e., the diluted mixture of all components) is from about 0.88% by weight or more as recited in previously pending claim 3. In fact, based on the information presented by Daggy et al., it is likely that the actual amount of calcium cation theoretically envisioned by Daggy et al. is far less. Further, it is clear that the actual amount of calcium cation in this hypothetical would be much less than the amount of greater than about 1.8% by weight, which is recited in amended claim 1. In addition, the diluted mixtures of Daggy et al. clearly do not contain at least one irritant ingredient in an amount capable of inducing skin irritation.

Based on the above, withdrawal of this rejection is respectfully requested.

The Second Rejection

Claims 1-3, 12, and 22 stand rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Ito et al. (U.S. Patent No. 5,709,849). This rejection is respectfully traversed and withdrawal thereof is requested.

Ito et al. was discussed in response to previous Office Actions. Those discussions are incorporated by reference herein. As noted, Ito et al. disclose cosmetic compositions purportedly having suppressed stickiness and which include a bivalent metal salt of organic acid. (*See* Col. 1, lines 28-35) In its broadest general discussion of actual amounts of bivalent metal salts of organic acids, the amount of the bivalent metal salt of the organic acid is stated to preferably be 0.001% by weight to 5% by weight, and more preferably 0.003% by weight to 3% by weight, of the total amount of the cosmetic composition. (*See* Col. 2, lines 35-38) Nevertheless, those compositions exemplified with a calcium-containing salt (e.g., calcium chloride) include at most only 0.5% by weight calcium-containing salt, which equates to calcium cation amounts of up to 0.18% at most. (*See* Examples 1 and 3 and Comparative Example 1)

Still further, claim 22 recites a composition "wherein said irritant ingredient comprises one or more of the group consisting of 1-pyrrolidone-5-carboxylic acid, capryloyl salicylic acid, α-hydroxy decanoic acid, α-hydroxy octanoic acid, gluconolactone, methoxypropyl gluconamide, oxalic acid, malic acid, tartaric acid, mandelic acid, benzylic acid, gluconic acid, pyruvic acid and phenol." Although the Examiner notes that Ito et al. discusses pyrrolidone-carboxylic acid, Ito et al. do not disclose the specific irritant ingredients recited in claim 22, which are present in composition of the invention in an amount capable of inducing skin irritation. For example, Ito et al. do not discuss use of 1-pyrrolidone-5-carboxylic acid as specifically recited in claim 22, despite there being some discussion of pyrrolidone carboxylic acid in general. Thus, withdrawal of this rejection with respect to claim 22 is again independently requested.

Nevertheless, in order to expedite prosecution, claim 1 has been amended to recite the minimum amount of calcium cation specified in claim 4 (a claim indicated to be patentable over Ito et al.). As claims 2-3, 12, and 22 ultimately depend from claim 1, those claims are also deemed to be patentable over Ito et al. – thus, overcoming this rejection. As such, withdrawal of this rejection in its entirety is respectfully requested.

The 35 U.S.C. §103(a) Rejection

The First Rejection

Claims 1-5, 7, 10, 12, 22, 24, and 116-119 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Daggy et al. (U.S. Patent No. 5,422,101). This rejection is respectfully traversed and withdrawal thereof is requested.

Amended claim 1 now recites a composition for topical application to an animal subject comprising: a topical vehicle; at least one irritant ingredient contained in an amount capable of inducing skin irritation in said subject; an anti-irritant amount of aqueous-soluble divalent calcium cation in a concentration of at least about 1.8% by weight; and at least one aqueous-ionizable counter-anionic species. Such compositions are not taught or suggested by Daggy et al.

The present rejection focuses on the asserted amounts of metal salt within the compositions of Daggy et al. However, as noted in discussing the rejection over Daggy et al. under 35 U.S.C. §102(e), the compositions of Daggy et al. also do not contain an irritant ingredient in an amount capable of inducing skin irritation. Indeed, the diluted mixtures of all components (the compositions taught by Daggy et al. to be for consumption) contained only negligible amounts of acid (a component that is apparently argued by the Patent Office to be the irritant ingredient of presently claimed compositions). Thus, the presently claimed invention is distinguishable from Daggy et al. for that further reason as well.

Nevertheless, for the reasons also discussed above in responding to the rejection over Daggy et al. under 35 U.S.C. §102(e), the amount of calcium cation in the compositions of Daggy et al. falls far short of the amounts presently claimed - at least about 1.8% by weight of the composition as recited in amended claim 1. Again, it is to be noted that the referenced weight percentages in the disclosure of Daggy et al. are associated only with drink mix compositions therein – not compositions that are dispersed in an aqueous solution such that they are ready for ingestion by an individual. The actual amounts of each of these two components in the final aqueous solution are much lower as discussed with the Examiner during the telephone interview.

Based on the above, withdrawal of this rejection is respectfully requested.

The Second Rejection

Claims 1-3, 12, and 22 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Ito et al. (U.S. Patent No. 5,709,849). This rejection is respectfully traversed and withdrawal thereof is respectfully requested.

Again, for the reasons discussed above in responding to the rejection over Ito et al. under 35 U.S.C. §102(e), the amount of calcium cation in the compositions of Ito et al. falls far short of the amounts presently claimed - at least about 1.8% by weight of the composition as recited in amended claim 1. Since claim 1 has been amended to recite the minimum amount of calcium cation specified in claim 4 (a claim indicated to be patentable over Ito et al.) in order to expedite prosecution, this rejection is now moot due

to the Patent Office's indication that claim 4 is patentable over Ito et al. As claims 2-3, 12, and 22 ultimately depend from claim 1, those claims are also deemed to be patentable over Ito et al. – thus, overcoming this rejection. As such, withdrawal of this rejection in its entirety is respectfully requested.

The Third Rejection

Claims 1-5, 7, 10-18, 21-25, 55, 57-58, 61, and 115-119 stand rejected under 35 U.S.C. §103(e) as allegedly being obvious over Mishima et al. (U.S. Patent No. 5,262,153) in view of Ito et al. (U.S. Patent No. 5,709,849), Giddey et al. (U.S. Patent No. 5,053,219), Cook et al. (U.S. Patent No. 2,719,811), and Henderson (U.S. Patent No. 5,296,476). This rejection is respectfully traversed.

For reasons discussed in response to previous Office Actions, Applicants question the propriety of this rejection, which is notably based on a combination of five different documents. Nevertheless, even if the five documents are properly combineable as suggested by the Examiner, the Patent Office's asserted combination does not teach or suggest all of the claim elements.

The asserted combination of Mishima et al. with the four secondary references does not overcome Mishima et al.'s deficiencies. The Examiner's currently cited primary document, Mishima et al., was discussed by Applicants in the description of the invention. See page 8, lines 1-9, of the application as filed. As discussed therein, Mishima et al. did not recognize any need or ability to reduce irritation effects in the skin-whitening agents described therein. The skin-whitening agents therein are stated to be lactic acid and its derivatives as well as lactates of alkali metal or alkaline earth metals at a concentration of 5% by weight or higher.

The present rejection focuses on Mishima et al.'s exemplification of calcium lactate as a skin-whitening agent. However, Mishima et al. do not teach compositions having the specific combination of calcium lactate and lactic acid, both of which are independently referred to as skin-whitening agents. See, for example, claims 1-3 of Mishima et al. Notably, the presently rejected claims recite compositions comprising both an irritant ingredient and an anti-irritant amount of aqueous-soluble calcium cation.

Mishima et al.'s mention of calcium lactate does not satisfy the requirement set forth in the presently rejected claims that the compositions therein contain both recited components. The Examiner's reliance on the asserted combination of Mishima et al. with four secondary references does not overcome this deficiency. Thus, the asserted combination of Mishima et al. with the four additional secondary references fails to satisfy the minimum Patent Office requirements needed in order to sustain a prima facie case of obviousness. Withdrawal of this rejection is thus requested.

In view of the foregoing, allowance of all pending claims is respectfully requested. If deemed useful in order to further prosecution of this application to allowance, the Examiner is invited to contact the undersigned by telephone, e-mail, facsimile, or written communication.

Respectfully Submitted,

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